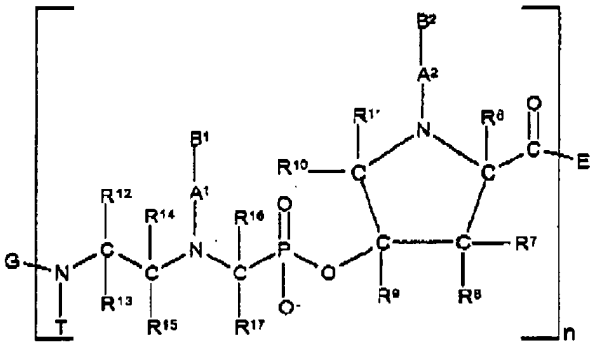
USSN: 10/072,975 8 SEPT 2004

AMENDMENT

In the claims

1-29. (canceled)

30. (original) A method for inhibiting gene expression, comprising administering an oligonucleotide analogue to at least one cell or at least one organism to inhibit expression of at least one gene that comprises a nucleotide sequence that is at least partially complementary to the oligonucleotide analogue, wherein the oligonucleotide analogue comprises the structure:



wherein G is selected from a group consisting of H and is a protecting group;

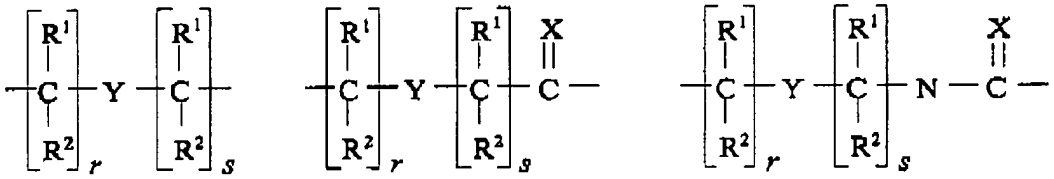
wherein E is selected from a group consisting of O-, OH, a protecting group, and an activating group;

wherein n is 1 or greater;

wherein each B^1 and B^2 is independently selected from the group consisting of H, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic

moiety, a DNA intercalator, a heterocyclic moiety, and a reporter group, wherein amino groups, if present, are, optionally, protected by amino protecting groups;

wherein each A^1 and A^2 is independently selected from the group ~~of~~ consisting of formula (Ia), ~~and~~ (Ib), and (Ic):



I(a) I(b) I(c)

wherein each R^1 and R^2 is independently selected from the group of consisting of hydrogen; (C_1 –C_6)alkyl; hydroxy-, alkoxy-, amino-, or alkythio-substituted (C_1 – C_6)alkyl; hydroxy; alkoxy; alkylthio; amino; and halogen;

wherein r and s are, for I(a), ~~and~~ I(b), and I(c) independently of one another, values from 0 to 5;

Y is a single bond, O, S, or NR^4;

X is O, S, Se, NR^5, CH_2, or $C(CH_3)_2$; and

wherein each R^4 and R^5 is independently selected from the group of consisting of hydrogen; (C_1 –C_6)alkyl; hydroxy-, alkoxy-, amino-, or alkythio-substituted (C_1 – C_6)alkyl; hydroxy; alkoxy; amino; aryl; aralkyl; heteroaryl; and an amino acid side chain;

wherein each R^6 is independently selected from the group of consisting of hydrogen; (C_1 –C_6)alkyl; hydroxy-, alkoxy-, amino-, or alkythio-substituted (C_1 –C_6)alkyl; aryl; aralkyl; heteroaryl; and an amino acid side chain;

wherein each R^7 is independently selected from the group of consisting of hydrogen; (C_1 –C_6)alkyl; hydroxy-, alkoxy-, amino-, or alkythio-substituted (C_1 –C_6)alkyl; hydroxy; alkoxy; alkylthio; amino; aryl; aralkyl; and heteroaryl; and each R^8 is independently selected from the group of consisting of hydrogen; (C_1 –C_6) alkyl; hydroxy-, alkoxy-, amino-, or alkythio-substituted (C_1 –C_6)alkyl; aryl; aralkyl; and heteroaryl; or

wherein each R^7 is independently selected from the group of consisting of hydrogen; (C_1 –C_6)alkyl; hydroxy-, alkoxy-, amino-, or alkythio-substituted (C_1 –C_6)alkyl; aryl; aralkyl; and heteroaryl; and R^8 is independently selected from the group of consisting of hydrogen; (C_1 –C_6)alkyl; hydroxy-, alkoxy-, amino-, or alkythio-substituted (C_1 –C_6)alkyl; hydroxy; alkoxy; alkylthio; amino; aryl; aralkyl; heteroaryl; and halogen;

wherein each R^9 is independently selected from the group of consisting of hydrogen; (C_1 –C_6)alkyl; hydroxy-, alkoxy-, amino-, or alkythio-substituted (C_1 –C_6)alkyl; alkoxy; aryl; arylkyl; and heteroaryl;

wherein each R^{10} and R^{11} is independently selected from the group of consisting of hydrogen; (C_1 –C_6)alkyl; hydroxy-, alkoxy-, amino-, or alkythio-substituted (C_1 –C_6)alkyl; aryl; aralkyl; heteroaryl; and an amino acid side chain;

wherein each R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, and R^{17} is independently selected from the group of consisting of hydrogen; (C_1 –C_6)alkyl; hydroxy-, alkoxy-, amino-, or alkythio-substituted (C_1 –C_6)alkyl; hydroxy; alkoxy; alkylthio; aryl; aralkyl; heteroaryl; and an amino acid side chain; and

wherein each T is independently selected from the group of consisting of hydrogen; (C_1 – C_6)alkyl; hydroxy-, alkoxy-, amino-, or alkythio-substituted (C_1 –C_6)alkyl; hydroxy; alkoxy; alkylthio; aryl; aralkyl; heteroaryl; and an amino acid side chain;

and salts thereof.

31. (original) A method according to claim 30 wherein n is less than about 500.

32. (original) A method according to claim 30 wherein n is less than about 50.

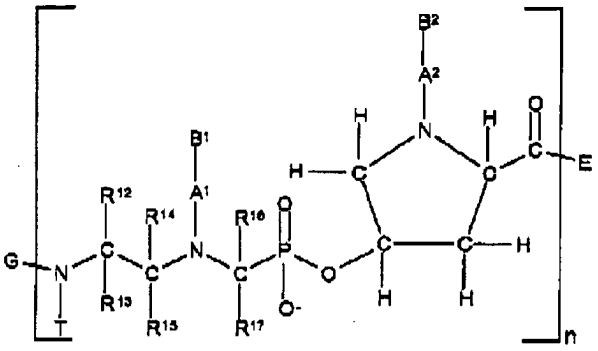
33. (original) A method according to claim 30 wherein n is less than about 15.

34. (original) A method according to claim 30 wherein n is selected from the group consisting of 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, and 15.

35. (currently amended) A method according to claim 31 wherein said oligonucleotide analogue comprises a ratio of HypNA to pPNA monomers and wherein the ratio of HypNA to pPNA monomers in the oligonucleotide analogue is from about 2:1 to about 1:3.

36. (currently amended) A method according to claim 31 wherein said oligonucleotide analogue comprises a ratio of HypNA to pPNA monomers and wherein the ratio of HypNA to pPNA monomers in the oligonucleotide analogue is from about 1:1 to about 1:2.

37. (original) A method for inhibiting gene expression, comprising administering an oligonucleotide analogue to at least one cell or at least one organism to inhibit expression of at least one gene that comprises a nucleotide sequence that is at least partially complementary to the oligonucleotide analogue, wherein the oligonucleotide analogue comprises the structure:



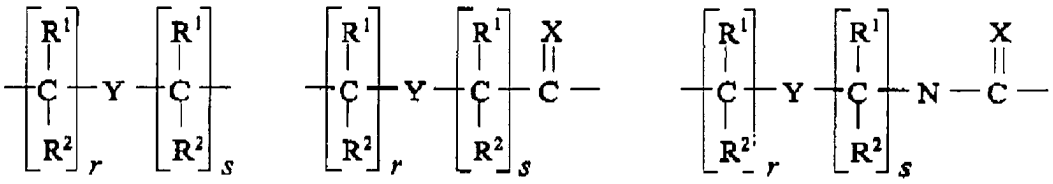
wherein G is selected from a group consisting of H and is a protecting group;

wherein E is selected from a group consisting of O-, OH, a protecting group, and an activating group;

wherein n is 1 or greater;

wherein each B^1 and B^2 is independently selected from the group consisting of H, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a heterocyclic moiety, and a reporter group, wherein amino groups, if present, are, optionally, protected by amino protecting groups;

wherein each A^1 and A^2 is independently selected from the group of consisting of formula (Ia), ~~and~~ (Ib), and (Ic):



I(a) I(b) I(c)

wherein each R^1 and R^2 is independently selected from the group of consisting of

hydrogen; (C_1 –C_6)alkyl; hydroxy-, alkoxy-, amino-, or alkythio-substituted (C_1 – C_6)alkyl; hydroxy; alkoxy; alkylthio; amino; and halogen;

wherein *r* and *s* are, for I(a), ~~and~~ (Ib), and (Ic) independently of one another, values from 0 to 5;

Y is a single bond, O, S, or NR^4;

X is O, S, Se, NR^5, CH_2, or $C(CH_3)_2$; and

wherein each R^4 and R^5 is independently selected from the group of consisting of hydrogen; (C_1 –C_6)alkyl; hydroxy-, alkoxy-, amino-, or alkythio-substituted (C_1 – C_6)alkyl; hydroxy; alkoxy; amino; aryl; aralkyl; heteroaryl; and an amino acid side chain;

wherein each R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, and R^{17} is independently selected from the group of consisting of hydrogen; (C_1 –C_6)alkyl; hydroxy-, alkoxy-, amino-, or alkythio-substituted (C_1 –C_6)alkyl; hydroxy; alkoxy; alkylthio; aryl; aralkyl; heteroaryl; and an amino acid side chain; and

wherein each T is independently selected from the group of consisting of hydrogen; (C_1 – C_6)alkyl; hydroxy-, alkoxy-, amino-, or alkythio-substituted (C_1 –C_6)alkyl; hydroxy; alkoxy; alkylthio; aryl; aralkyl; heteroaryl; and an amino acid side chain;

and salts thereof.

38. (currently amended) A method according to claim 37 wherein n is less than about 500.

39. (original) A method according to claim 37 wherein n is less than about 50.

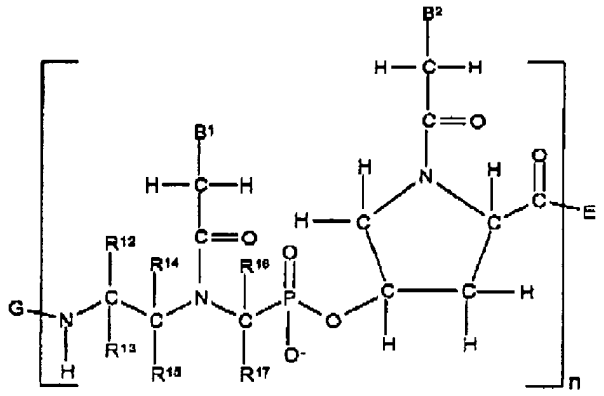
40. (original) A method according to claim 37 wherein n is less than about 15.

41. (original) A method according to claim 37 wherein n is selected from the group consisting of 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, and 15.

42. (currently amended) A method according to claim 38 wherein said oligonucleotide analogue comprises a ratio of HypNA to pPNA monomers and wherein the ratio of HypNA to pPNA monomers in the oligonucleotide analogue is from about 2:1 to about 1:3.

43. (currently amended) A method according to claim 38 wherein said oligonucleotide analogue comprises a ratio of HypNA to pPNA monomers and wherein the ratio of HypNA to pPNA monomers in the oligonucleotide analogue is from about 1:1 to about 1:2.

44. (original) A method for inhibiting gene expression, comprising administering an oligonucleotide analogue to at least one cell or at least one organism to inhibit expression of at least one gene that comprises a nucleotide sequence that is at least partially complementary to the oligonucleotide analogue, wherein the oligonucleotide analogue comprises the structure:



wherein G is selected from a group consisting of H and is a protecting group;

wherein E is selected from a group consisting of O-, OH, a protecting group, and an activating group;

wherein n is 1 or greater;

wherein each B^1 and B^2 is independently selected from the group consisting of H, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a heterocyclic moiety, and a reporter group, wherein amino groups, if present, are, optionally, protected by amino protecting groups;

wherein each R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, and R^{17} is independently selected from the group of consisting of hydrogen; (C_1 –C_6)alkyl; hydroxy-, alkoxy-, amino-, or alkythio-substituted (C_1 –C_6)alkyl; hydroxy; alkoxy; alkylthio; aryl; aralkyl; heteroaryl; and an amino acid side chain; and

wherein each T is independently selected from the group of consisting of hydrogen; (C_1 – C_6)alkyl; hydroxy-, alkoxy-, amino-, or alkythio-substituted (C_1 –C_6)alkyl; hydroxy; alkoxy; alkylthio; aryl; aralkyl; heteroaryl; and an amino acid side chain;

and salts thereof.

45. (original) A method according to claim 44 wherein n is less than about 500.

46. (original) A method according to claim 44 wherein n is less than about 50.

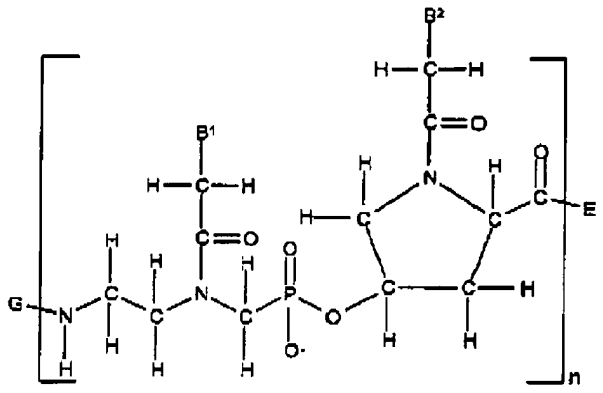
47. (original) A method according to claim 44 wherein n is less than about 15.

48. (original) A method according to claim 44 wherein n is selected from the group consisting of 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, and 15.

49. (currently amended) A method according to claim 45 wherein said oligonucleotide analogue comprises a ratio of HypNA to pPNA monomers and wherein the ratio of HypNA to pPNA monomers in the oligonucleotide analogue is from about 2:1 to about 1:3.

50. (currently amended) A method according to claim 45 wherein said oligonucleotide analogue comprises a ratio of HypNA to pPNA monomers and wherein the ratio of HypNA to pPNA monomers in the oligonucleotide analogue is from about 1:1 to about 1:2.

51. (original) A method for inhibiting gene expression, comprising administering an oligonucleotide analogue to at least one cell or at least one organism to inhibit expression of at least one gene that comprises a nucleotide sequence that is at least partially complementary to the oligonucleotide analogue, wherein the oligonucleotide analogue comprises the structure:



wherein G is selected from a group consisting of H and is a protecting group;

wherein E is selected from a group consisting of O-, OH, a protecting group, and an activating group;

wherein n is 1 or greater;

wherein each B^1 and B^2 is independently selected from the group consisting of H, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a heterocyclic moiety, and a reporter group, wherein amino groups, if present, are, optionally, protected by amino protecting groups; and

wherein each T is independently selected from the group of consisting of hydrogen; (C_1 – C_6)alkyl; hydroxy-, alkoxy-, amino-, or alkythio-substituted (C_1 –C_6)alkyl; hydroxy; alkoxy; alkylthio; aryl; aralkyl; heteroaryl; and an amino acid side chain;

and salts thereof.

52. (original) A method according to claim 51 wherein n is less than about 500.

53. (original) A method according to claim 51 wherein n is less than about 50.

54. (original) A method according to claim 51 wherein n is less than about 15.

55. (original) A method according to claim 51 wherein n is selected from the group consisting of 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, and 15.

56. (currently amended) A method according to claim 52 wherein said oligonucleotide analogue comprises a ratio of HypNA to pPNA monomers and wherein the ratio of HypNA to pPNA monomers in the oligonucleotide analogue is from about 2:1 to about 1:3.

57. (currently amended) A method according to claim 52 wherein said oligonucleotide analogue comprises a ratio of HypNA to pPNA monomers and wherein the ratio of HypNA to pPNA monomers in the oligonucleotide analogue is from about 1:1 to about 1:2.